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72878

Access DB# \_\_\_\_\_

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: RICHARD SCHWIZER Examiner #: 76557 Date: 8/8/02  
Art Unit: 1635 Phone Number 306-5441 Serial Number: 09/786 055  
Mail Box and Bldg/Room Location: 11E12 Results Format Preferred (circle): PAPER DISK E-MAIL

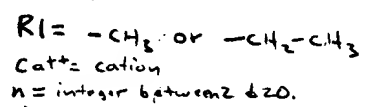
If more than one search is submitted, please prioritize searches in order of need.  
\*\*\*\*\*  
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: PHOSPHOEPOXIDES  
Inventors (please provide full names): CHRISTIAN BELMANT, JEAN-JACQUE FOURNIE, MARC BONNEVILLE,  
MARIE-ALIX PEYRAT

Earliest Priority Filing Date: 9/1/98

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for the following structures:



R1, cat, and  
n, and  
above

STAFF USE ONLY		Type of Search	Vendors and cost where applicable
Searcher: <u>Point of Contact</u>	NA Sequence (#) _____	STN <u>320 00</u>	
Searcher Phone: <u>Alexandra Wadaw</u>	AA Sequence (#) _____	Dialog _____	
Searcher Location: <u>Technical Info. Specialist</u>	Structure (#) <u>1</u>	Questel/Orbit _____	
CM1 8A02 Tel: 308-4491	Bibliographic <u>h</u>	Dr. Link _____	
Date Searcher Picked Up: <u>8-12-02</u>	Litigation <u>h</u>	Lexis/Nexis _____	
Date Completed: <u>8-12-02</u>	Fulltext <u>h</u>	Sequence Systems _____	
Searcher Prep & Review Time: <u>18</u>	Patent Family <u>h</u>	WWW/Internet _____	
Clerical Prep Time: _____	Other _____	Other (specify) _____	
Online Time: <u>38</u>			

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(FILE 'HCAOLD' ENTERED AT 09:03:30 ON 12 AUG 2002)  
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FILE 'REGISTRY' ENTERED AT 09:04:05 ON 12 AUG 2002  
ACT RICHARD/A

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L1 STR  
L2 45 SEA FILE=REGISTRY SSS FUL L1  
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L3 1 S 1492-08-6  
L4 44 S L2 NOT L3  
L5 33 S L4 AND (CAPLUS OR CA)/LC  
L6 0 S L4 AND USPATFULL/LC

FILE 'HCAOLD' ENTERED AT 09:05:07 ON 12 AUG 2002

FILE 'HCAPLUS' ENTERED AT 09:05:21 ON 12 AUG 2002  
L7 15 S L2/P OR L2(L) (PREPN OR PREPAR? OR MANUF? OR MFG# OR PREP/RL)  
L8 17 S L4  
L9 22 S L7 OR L8

FILE 'HCAOLD' ENTERED AT 09:05:47 ON 12 AUG 2002  
L10 3 S L4

=> fil reg

FILE 'REGISTRY' ENTERED AT 09:05:57 ON 12 AUG 2002

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STRUCTURE FILE UPDATES: 9 AUG 2002 HIGHEST RN 443534-23-4

DICTIONARY FILE UPDATES: 9 AUG 2002 HIGHEST RN 443534-23-4

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

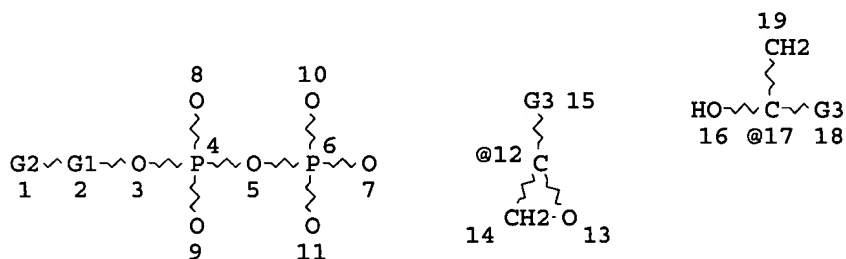
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L1 STR



REP G1=(2-20) CH2

VAR G2=12/17

VAR G3=ME/ET

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L2 45 SEA FILE=REGISTRY SSS FUL L1

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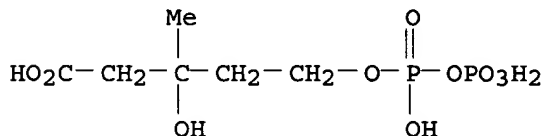
45 ANSWERS

SEARCH TIME: 00.00.07

=> d que 13;d 13

L3 1 SEA FILE=REGISTRY ABB=ON PLU=ON 1492-08-6

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
 RN 1492-08-6 REGISTRY  
 CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
 1,3-dioxide (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Pyrophosphoric acid, 5-ester with 3,5-dihydroxy-3-methylvaleric acid (8CI)  
 CN Valeric acid, 3,5-dihydroxy-3-methyl-, 5-(trihydrogen pyrophosphate) (8CI)  
 CN Valeric acid, 3,5-dihydroxy-3-methyl-, 5-pyrophosphate (6CI, 7CI)  
 OTHER NAMES:  
 CN 5-Pyrophosphomevalonic acid  
 CN Mevalonic 5-pyrophosphate  
 CN Mevalonic acid 5-diphosphate  
 CN Mevalonic acid 5-pyrophosphate  
 CN Mevalonic acid pyrophosphate  
 CN Pyrophosphomevalonic acid  
 FS 3D CONCORD  
 MF C6 H14 O10 P2  
 CI COM  
 LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAOLD, CAPLUS, TOXCENTER  
 (\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

55 REFERENCES IN FILE CA (1967 TO DATE)  
 55 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

→ one of the  
 answers from struct.  
 search. ~~used~~  
 Too many references.  
 See L4

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(FILE 'REGISTRY' ENTERED AT 09:04:05 ON 12 AUG 2002)  
 L4 44 S L2 NOT L3

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 09:06:25 ON 12 AUG 2002

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structure search minus above structure  
 (used to limit number of references)

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FILE COVERS 1907 - 12 Aug 2002 VOL 137 ISS 7

FILE LAST UPDATED: 11 Aug 2002 (20020811/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.  
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L2      45 SEA FILE=REGISTRY SSS FUL L1
L3      1 SEA FILE=REGISTRY ABB=ON PLU=ON 1492-08-6
L4      44 SEA FILE=REGISTRY ABB=ON PLU=ON L2 NOT L3
L7      15 SEA FILE=HCAPLUS ABB=ON PLU=ON L2/P OR L2(L) (PREPN/OBI OR
        PREPAR?/OBI OR MANUF?/OBI OR MFG#/OBI OR PREP/RL)
L8      17 SEA FILE=HCAPLUS ABB=ON PLU=ON L4
L9      22 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 OR L8
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L9  ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:    2002:451578  HCAPLUS
DOCUMENT NUMBER:     137:61783
TITLE:               Synaptic transfer by human .gamma..delta. T cells
                     stimulated with soluble or cellular antigens
AUTHOR(S):           Espinosa, Eric; Tabiasco, Julie; Hudrisier, Denis;
                     Fournie, Jean-Jacques
CORPORATE SOURCE:    Institut National de la Sante et de la Recherche
                     Medicale, Centre Hospitalier Universitaire Purpan,
                     Toulouse, 31024, Fr.
SOURCE:              Journal of Immunology (2002), 168(12), 6336-6343
                     CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER:           American Association of Immunologists
DOCUMENT TYPE:       Journal
LANGUAGE:            English
AB  B, .alpha..beta. T, and NK lymphocytes establish immunol. synapses (IS)
    with their targets to enable recognition. Transfer of target cell-derived
    Ags together with proximal mols. onto the effector cell appears also to
    occur through synapses. Little is known about the mol. basis of this
    transfer, but it is assumed to result from Ag receptor internalization.
    Because human .gamma..delta. T cells recognize sol. non-peptidic
    phosphoantigens as well as tumor cells such as Daudi, it is unknown
    whether they establish IS with, and ext. mols. from, target cells. Using
    flow cytometry and confocal microscopy, the authors show in this work that
    Ag-stimulated human V.gamma.9/V.delta.2 T cells conjugate to, and perform
    mol. transfer from, various tumor cell targets. The mol. transfer appears
    to be linked to IS establishment, evolves in a dose-dependent manner in
    the presence of either sol. or cellular Ag, and requires .gamma..delta.
    TCR ligation, Src family kinase signaling, and participation of the actin
    cytoskeleton. Although CD45 exclusion characterized the IS performed by
    .gamma..delta. T cells, no obvious capping of the .gamma..delta. TCR was
    detected. The synaptic transfer mediated by .gamma..delta. T cells
    involved target mols. unrelated to the cognate Ag and occurred
    independently of MHC class I expression by target cells. From these
    observations, the authors conclude that despite the particular features of
    .gamma..delta. T cell activation, both synapse formation and mol. transfer
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of determinants belonging to target cell characterize .gamma..delta. T cell recognition of Ags.

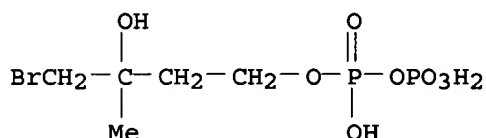
CC 15-2 (Immunochemistry)

IT 358-71-4, Isopentenyl pyrophosphate 252663-87-9 303102-05-8  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (synaptic transfer from target cell to human .gamma..delta. T-cells stimulated with)

IT 303102-05-8  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (synaptic transfer from target cell to human .gamma..delta. T-cells stimulated with)

RN 303102-05-8 HCAPLUS

CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:463707 HCAPLUS

DOCUMENT NUMBER: 135:207791

TITLE: Characterization of Phosphoantigens by High-Performance Anion-Exchange Chromatography-Electrospray Ionization Ion Trap Mass Spectrometry and Nanoelectrospray Ionization Ion Trap Mass Spectrometry  
 AUTHOR(S): Pont, Frederic; Luciani, Beatrice; Belmant, Christian; Fournie, Jean Jacques

CORPORATE SOURCE: Service de Spectrometrie de Masse de l'IFR 30, CHU Purpan, Toulouse, 31024, Fr.

SOURCE: Analytical Chemistry (2001), 73(15), 3562-3569  
 CODEN: ANCHAM; ISSN: 0003-2700

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB New phosphorylated microbial metabolites referred to as phosphoantigens activate immune responses in humans. Although these mols. have leading applications in medical research, no direct method allows their rapid and unambiguous structural identification. Here, we interfaced online high performance anion-exchange chromatog. (HPAEC) with electrospray ionization ion trap mass spectrometry (ESI-ITMS) to identify such pyrophosphorylated mols. A self-regenerating anion suppressor located upstream of electrospray ionization enabled the simultaneous detection of pyrophosphoester by conductimetry, UV and MS. By HPAEC-ITMS and HPAEC-ITMS2, a single run permitted characterization of ref. phosphoantigens and of related structures. Although all compds. were resolved by HPAEC, MS enabled their detection and identification by [M - H]- and fragment ions. Isobaric phosphoantigen analogs were also sepd. by HPAEC and distinguished by MS2. The relevance of this device was demonstrated for phosphoantigens anal. in human urine and plasma. Furthermore, identification of natural phosphoantigens by automatically generated 2D mass spectra from nano-ESI-ITMS is presented. This last technique permits the simultaneous performance of mol. screening of

natural phosphoantigen exts. and their identification.

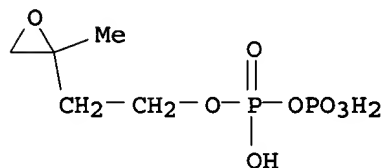
CC 9-16 (Biochemical Methods)  
Section cross-reference(s): 15

IT 358-71-4 372-97-4, Farnesyl pyrophosphate 763-10-0, Geranyl pyrophosphate 96555-67-8 **115914-67-5** 357426-54-1  
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)  
(characterization of phosphoantigens by anion-exchange HPLC-electrospray ionization ion trap mass spectrometry and nanoelectrospray ionization ion trap mass spectrometry)

IT **115914-67-5**  
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)  
(characterization of phosphoantigens by anion-exchange HPLC-electrospray ionization ion trap mass spectrometry and nanoelectrospray ionization ion trap mass spectrometry)

RN 115914-67-5 HCAPLUS

CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:411550 HCAPLUS

DOCUMENT NUMBER: 135:179341

TITLE: Chemical synthesis and biological activity of bromohydrin pyrophosphate, a potent stimulator of human .gamma..delta. T cells

AUTHOR(S): Espinosa, Eric; Belmant, Christian; Pont, Frederic; Luciani, Beatrice; Poupot, Remy; Romagne, Francois; Brailly, Herve; Bonneville, Marc; Fournie, Jean-Jacques

CORPORATE SOURCE: INSERM U395, CHU Purpan, Toulouse, 31024, Fr.  
SOURCE: Journal of Biological Chemistry (2001), 276(21), 18337-18344

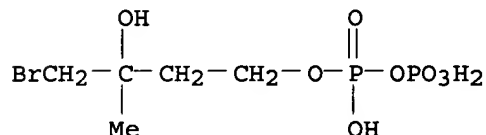
PUBLISHER: CODEN: JBCHA3; ISSN: 0021-9258  
American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Small phosphorylated metabolites from mycobacteria stimulate human .gamma..delta. T lymphocytes. Although such phosphoantigens could prove useful in the compn. of vaccines involving .gamma..delta. T cell-mediated immunity, their very low abundance in natural sources limits such applications. Here, we describe the chem. prodn., purifn., and bioactivity of a phosphorylated bromohydrin (BrHPP) analog that mimics the biol. properties of natural phosphoantigens. This compd. can be obtained in gram amts., is easy to detect, and is of high stability in aq. solns. Whereas unspecific binding of BrHPP to a wide panel of cell surface receptors is not detected even at micromolar concns., nanomolar concns. specifically trigger effector responses of human .gamma..delta. T lymphocytes. Thus, BrHPP is a novel mol. enabling potent

immunostimulation of human .gamma..delta. T lymphocytes.  
 CC 15-2 (Immunochemistry)  
 IT 303102-05-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**  
 (chem. synthesis and biol. activity of bromohydrin pyrophosphate, a potent stimulator of human .gamma..delta. T cells)  
 IT 303102-05-8P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**  
 (chem. synthesis and biol. activity of bromohydrin pyrophosphate, a potent stimulator of human .gamma..delta. T cells)  
 RN 303102-05-8 HCAPLUS  
 CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:401111 HCAPLUS

DOCUMENT NUMBER: 135:165761

TITLE: Differential activation of human .gamma..delta. cells by nonpeptide phosphoantigens

AUTHOR(S): Sireci, Guido; Espinosa, Eric; Di Sano, Caterina; Dieli, Francesco; Fournie, Jean-Jacques; Salerno, Alfredo

CORPORATE SOURCE: Department of Biopathology, University of Palermo, Palermo, Italy

SOURCE: European Journal of Immunology (2001), 31(5), 1628-1635

CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

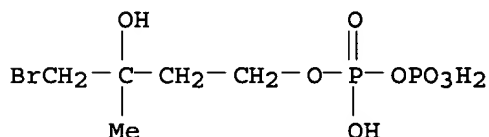
LANGUAGE: English

AB Human T cells expressing V.gamma.9/V.delta.2-encoded TCR recognize several nonpeptide phosphoantigens in the absence of major histocompatibility complex restriction. As these cells respond differentially to increasing concns. of structurally related phosphoantigens, such ligands constitute agonists of different strengths. By analyzing early cellular events and late effector responses of .gamma..delta. T cells, we compared their patterns of stimulation by weak, medium and strong phosphoantigen agonists. We found that, although the early metabolic activation as assessed by cytosensor microphysiometry directly reflects the intensity of subsequent effector response by .gamma..delta. cells, TCR down-modulation is dissocd. from the latter. Weak and mid-range phosphoantigen agonists induce a time- and dose-dependent down-modulation of the .gamma..delta. TCR, whereas strong phosphoantigen agonists induce little or no TCR down-regulation. This indicates that .gamma..delta. TCR down-modulation does not match the extent of TCR signaling as assessed by microphysiometry



or conventional effector responses (TNF-.alpha. prodn. and cytotoxicity). This differential pattern of .gamma..delta. cell activation by phosphoantigens could explain the stronger potencies of some of these agonists.

CC 15-2 (Immunochemistry)  
 IT 358-71-4, Isopentenyl pyrophosphate 21317-51-1 252663-87-9  
 303102-05-8  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (differential activation of human .gamma..delta. cells by nonpeptide phosphoantigens)  
 IT 303102-05-8  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (differential activation of human .gamma..delta. cells by nonpeptide phosphoantigens)  
 RN 303102-05-8 HCAPLUS  
 CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:119873 HCAPLUS

DOCUMENT NUMBER: 137:92275

TITLE: A chemical basis for selective recognition of nonpeptide antigens by human .delta. T cells. [Erratum to document cited in CA133:320819]

AUTHOR(S): Belmant, Christian; Espinosa, Eric; Halary, Franck; Tang, Yong; Peyrat, Marie-Alix; Sicard, Helene; Kozikowski, Aalan; Buelow, Roland; Poupot, Remy; Bonneville, Marc; Fournie, Jean-Jacques

CORPORATE SOURCE: INSERM U395, CHU Purpan, Toulouse, 31024, Fr.

SOURCE: FASEB Journal (2000), 14(13), 2128

CODEN: FAJOEC; ISSN: 0892-6638

URL: <http://www.fasebj.org/cgi/doi/10.1096/fj.99-0909fje>

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The correct URL link (web address) is <http://www.fasebj.org/cgi/doi/10.1096/fj.99-0909fje>.

CC 15-2 (Immunochemistry)

IT 358-71-4, Isopentenyl pyrophosphate 2920-99-2 115914-67-5

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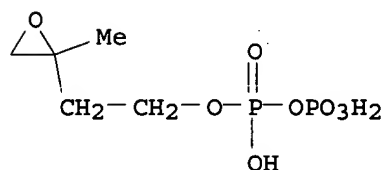
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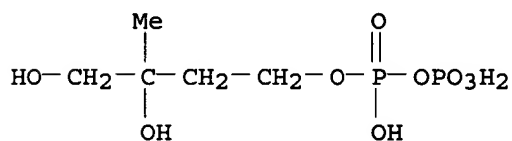
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(structure-function anal. of T-cell recognition of (Erratum))

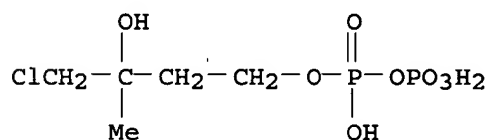
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 (Biological study)  
 (structure-function anal. of T-cell recognition of (Erratum))  
 RN 115914-67-5 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX  
 NAME)



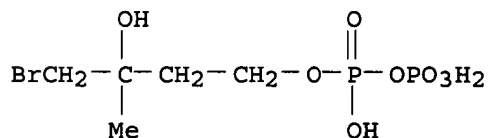
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 CN Diphosphoric acid, mono(3,4-dihydroxy-3-methylbutyl) ester (9CI) (CA  
 INDEX NAME)



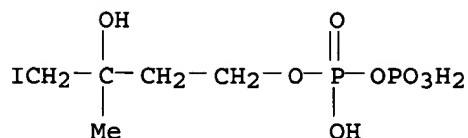
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RN 303102-05-8 HCAPLUS  
 CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester (9CI) (CA  
 INDEX NAME)



RN 303102-06-9 HCAPLUS  
 CN Diphosphoric acid, mono(3-hydroxy-4-iodo-3-methylbutyl) ester (9CI) (CA  
 INDEX NAME)



L9 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:655984 HCAPLUS

DOCUMENT NUMBER: 133:320819

TITLE: A chemical basis for selective recognition of

AUTHOR(S): nonpeptide antigens by human .delta. T cells  
 Belmant, Christian; Espinosa, Eric; Halary, Franck;  
 Tang, Yong; Peyrat, Marie-Alix; Sicard, Helene;  
 Kozikowski, Alan; Buelow, Roland; Poupot, Remy;  
 Bonneville, Marc; Fournie, Jean-Jacques

CORPORATE SOURCE: INSERM U395, CHU Purpan, Toulouse, 31024, Fr.

SOURCE: FASEB Journal (2000), 14(12), 1669-1670

CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental  
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human .gamma..delta. T lymphocytes activate their immune function upon  
 TCR-mediated recognition of antigens not assocd. with MHC mols. Because  
 different non-peptide phosphorylated antigens (phosphoantigens) are  
 selectively recognized by .gamma..delta. T cells, the authors clarified  
 its mol. basis through the structure-function relation of novel synthetic  
 phosphoantigens.

CC 15-2 (Immunochemistry)

IT 303102-05-8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
 process); BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study); PROC (Process)

(structure-function anal. of T-cell recognition of)

IT 358-71-4, Isopentenyl pyrophosphate 2920-99-2 115914-67-5

202268-26-6 252663-87-9 303102-02-5 303102-03-6

303102-04-7 303102-06-9 303102-07-0 303102-08-1

303102-09-2 303102-10-5 303102-11-6

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(structure-function anal. of T-cell recognition of)

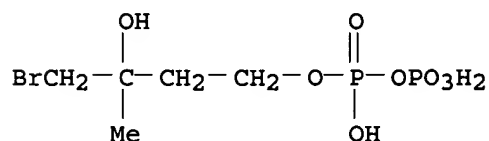
IT 303102-05-8

RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
 process); BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study); PROC (Process)

(structure-function anal. of T-cell recognition of)

RN 303102-05-8 HCAPLUS

CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester (9CI) (CA  
 INDEX NAME)



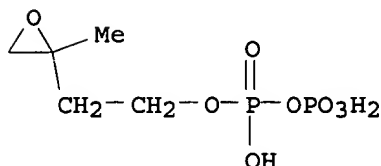
IT 115914-67-5 303102-03-6 303102-04-7

303102-06-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(structure-function anal. of T-cell recognition of)

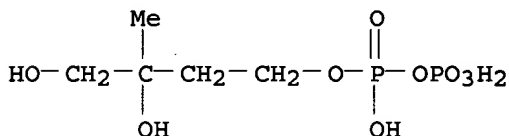
RN 115914-67-5 HCAPLUS

CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX NAME)



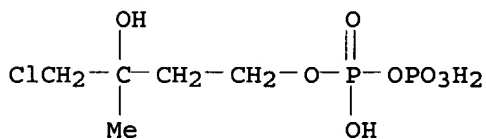
RN 303102-03-6 HCAPLUS

CN Diphosphoric acid, mono(3,4-dihydroxy-3-methylbutyl) ester (9CI) (CA INDEX NAME)



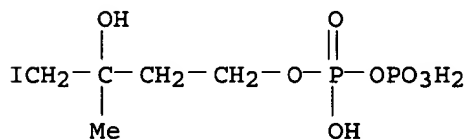
RN 303102-04-7 HCAPLUS

CN Diphosphoric acid, mono(4-chloro-3-hydroxy-3-methylbutyl) ester (9CI) (CA INDEX NAME)



RN 303102-06-9 HCAPLUS

CN Diphosphoric acid, mono(3-hydroxy-4-iodo-3-methylbutyl) ester (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:161295 HCAPLUS

DOCUMENT NUMBER: 132:194500

TITLE: Preparation of phosphoepoxides and their application

in activating T.gamma.9.delta.2 lymphocytes of  
primates  
INVENTOR(S): Belmant, Christian; Fournie, Jean-jacques; Bonneville,  
Marc; Peyrat, Marie-alix  
PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche  
Medicale, Fr.  
SOURCE: PCT Int. Appl., 52 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012519	A1	20000309	WO 1999-FR2057	19990827
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2782722	A1	20000303	FR 1998-10914	19980901
FR 2782722	B1	20010112		
AU 9954265	A1	20000321	AU 1999-54265	19990827
EP 1109818	A1	20010627	EP 1999-940246	19990827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002523515	T2	20020730	JP 2000-567540	19990827
PRIORITY APPLN. INFO.:				
			FR 1998-10914	A 19980901
			WO 1999-FR2057	W 19990827

OTHER SOURCE(S): CASREACT 132:194500

AB The invention concerns compds. comprising at least a phosphoepoxide group of formula  $R_1C(CH_2O)(CH_2)nOP(O)(O-Cat+)OP(O)(O-Cat+)O-$  ( $R_1 = Me, Et$ ;  $Cat+ = org. or mineral cation$ ;  $n = 2-20$ ). The invention also concerns their prepn. methods and applications, particularly in therapy and for activating T.gamma.9.delta.2 lymphocytes of primates. For example, the Na salt of 3,4-epoxy-3-methylbutyl diphosphate was prepd. in 4 steps: (1) prepn. of 3-methyl-3-butenyl tosylate from tosyl chloride and isopentenol; (2) prepn. of the ammonium salt of 3-methyl-3-butenyl diphosphate from tris(tetrabutylammonium) hydrogen pyrophosphate and 3-methyl-3-butenyl tosylate; (3) the bromination of the 3-methyl-3-butenyl diphosphate by bromine water; and (4) cyclization in aq. ammonia.

IC ICM C07F009-655

ICS C07H019-10; C12N005-06; A61K031-665; A61K049-00

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1

IT 259793-68-5P, 3,4-Epoxy-3-methylbutyl tetrasodium triphosphate

259793-69-6P, .alpha.,.gamma.-Bis(3,4-epoxy-3-methylbutyl)

trisodium triphosphate 259793-70-9P, .gamma.-(3,4-Epoxy-3-

methylbutyl) trisodium uridine-5'-triphosphate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); IMF (Industrial manufacture); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); **PREP**

(Preparation); USES (Uses)

(prepn. and activation of T.gamma.9.delta.2 lymphocytes by)

IT 259793-71-0P, Triammonium 3-(bromomethyl)-3-hydroxybutyl

diphosphate 259793-73-2P, Tetraammonium 3-(bromomethyl)-3-hydroxybutyl triphosphate 259793-75-4P, Triammonium .alpha.,.gamma.-bis(3-(bromomethyl)-3-hydroxybutyl) triphosphate 259793-77-6P, Triammonium .gamma.-(3-hydroxy-3-(iodomethyl)butyl) uridine 5'-triphosphate

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(**prepn.** and cyclization to epoxide)

IT 259793-67-4P, 3,4-Epoxy-3-methylbutyl trisodium diphosphate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP** (**Preparation**); USES (Uses)

(**prepn.**, toxicity and activation of T.gamma.9.delta.2 lymphocytes by)

IT 259793-68-5P, 3,4-Epoxy-3-methylbutyl tetrasodium triphosphate

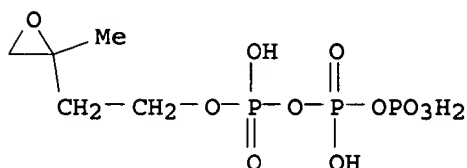
259793-69-6P, .alpha.,.gamma.-Bis(3,4-epoxy-3-methylbutyl) trisodium triphosphate 259793-70-9P, .gamma.-(3,4-Epoxy-3-methylbutyl) trisodium uridine-5'-triphosphate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP** (**Preparation**); USES (Uses)

(**prepn.** and activation of T.gamma.9.delta.2 lymphocytes by)

RN 259793-68-5 HCAPLUS

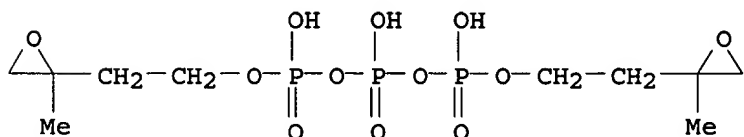
CN Triphosphoric acid, P-[2-(2-methyloxiranyl)ethyl] ester, tetrasodium salt (9CI) (CA INDEX NAME)



●4 Na

RN 259793-69-6 HCAPLUS

CN Triphosphoric acid, P,P''-bis[2-(2-methyloxiranyl)ethyl] ester, trisodium salt (9CI) (CA INDEX NAME)

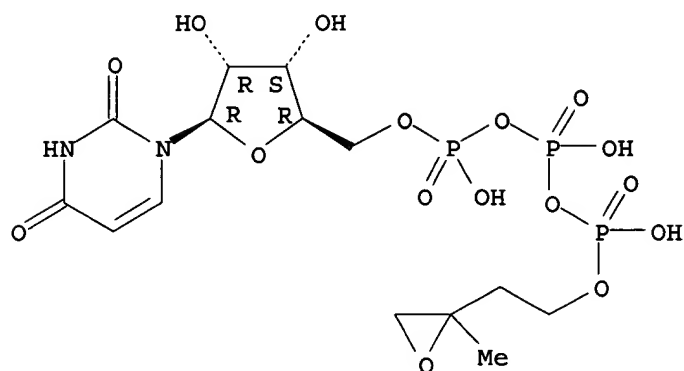


●3 Na

RN 259793-70-9 HCAPLUS

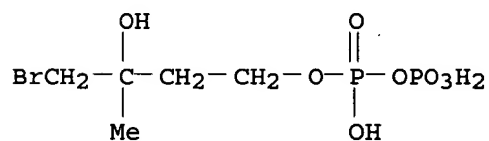
CN Uridine 5'-(tetrahydrogen triphosphate), P''-[2-(2-methyloxiranyl)ethyl] ester, trisodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



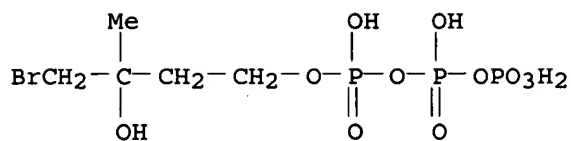
●3 Na

IT 259793-71-0P, Triammonium 3-(bromomethyl)-3-hydroxybutyl diphosphate 259793-73-2P, Tetraammonium 3-(bromomethyl)-3-hydroxybutyl triphosphate 259793-75-4P, Triammonium .alpha.,.gamma.-bis(3-(bromomethyl)-3-hydroxybutyl) triphosphate 259793-77-6P, Triammonium .gamma.-(3-hydroxy-3-(iodomethyl)butyl) uridine 5'-triphosphate  
 RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (**Preparation**); RACT (Reactant or reagent) (**prepn.** and cyclization to epoxide)  
 RN 259793-71-0 HCAPLUS  
 CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester, triammonium salt (9CI) (CA INDEX NAME)



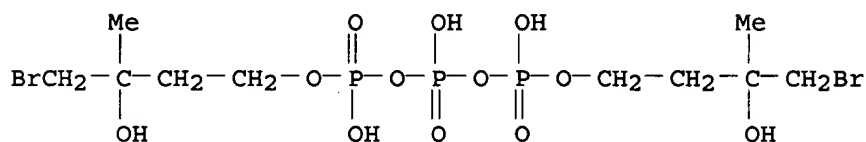
●3 NH<sub>3</sub>

RN 259793-73-2 HCAPLUS  
 CN Triphosphoric acid, P-(4-bromo-3-hydroxy-3-methylbutyl) ester, tetraammonium salt (9CI) (CA INDEX NAME)

● 4 NH<sub>3</sub>

RN 259793-75-4 HCAPLUS

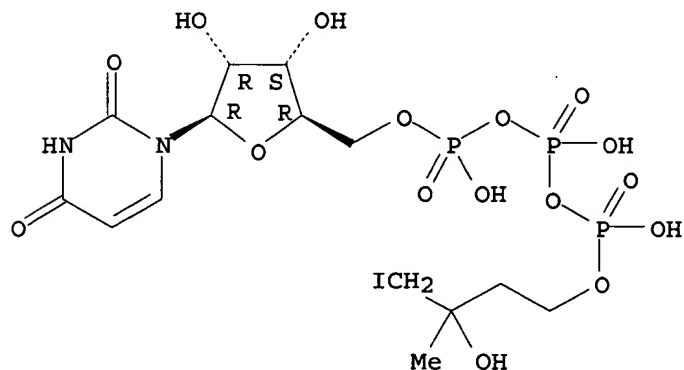
CN Triphosphoric acid, P,P''-bis(4-bromo-3-hydroxy-3-methylbutyl) ester, triammonium salt (9CI) (CA INDEX NAME)

● 3 NH<sub>3</sub>

RN 259793-77-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), P''-(3-hydroxy-4-iodo-3-methylbutyl) ester, triammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

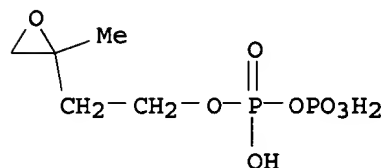
● 3 NH<sub>3</sub>

IT 259793-67-4P, 3,4-Epoxy-3-methylbutyl trisodium diphosphate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prep., toxicity and activation of T.gamma.9.delta.2)



lymphocytes by)  
 RN 259793-67-4 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester, trisodium salt  
 (9CI) (CA INDEX NAME)



● 3 Na

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:161292 HCAPLUS

DOCUMENT NUMBER: 132:194499

TITLE: Preparation of phosphohalohydrins and their applications in activating T.gamma.9.delta.2 lymphocytes of primates

INVENTOR(S): Belmant, Christian; Fournie, Jean-jacques; Bonneville, Marc; Peyrat, Marie-alix

PATENT ASSIGNEE(S): Institut National De La Sante Et De La Recherche Medicale, Fr.

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012516	A1	20000309	WO 1999-FR2058	19990827
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2782721	A1	20000303	FR 1998-10913	19980901
FR 2782721	B1	20001103		
AU 9954266	A1	20000321	AU 1999-54266	19990827
EP 1109817	A1	20010627	EP 1999-940247	19990827
EP 1109817	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 218576	E	20020615	AT 1999-940247	19990827
JP 2002523513	T2	20020730	JP 2000-567538	19990827
PRIORITY APPLN. INFO.:			FR 1998-10913	A 19980901

WO 1999-FR2058 W 19990827

OTHER SOURCE(S): CASREACT 132:194499

AB The invention concerns compds. comprising at least a phosphohalohydrin group of formula  $XCH_2CR_1(OH)(CH_2)_nOP(O)(O-Cat^+)OP(O)(O-Cat^+)O^-$  ( $X = I, Br, Cl$ ;  $R_1 = Me, Et$ ;  $Cat^+ = org. or mineral cation$ ;  $n = 2-20$ ). The invention also concerns their prepn. methods and applications, particularly in therapy and for activating T.gamma.9.delta.2 lymphocytes of primates. For example, the Na salt of 3-(bromomethyl)-3-hydroxybutyl diphosphate was prepd. in 3 steps: (1) prepn. of 3-methyl-3-butenyl tosylate from tosyl chloride and isopentenol; (2) prepn. of the ammonium salt of 3-methyl-3-butenyl diphosphate from tris(tetrabutylammonium) hydrogen pyrophosphate and 3-methyl-3-butenyl tosylate; and (3) the bromination of the 3-methyl-3-butenyl diphosphate by bromine water.

IC ICM C07F009-09

ICS C07H019-10; C12N005-06; A61K031-66; A61K049-00

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1

IT 259793-79-8P, 3-Hydroxy-3-(iodomethyl)butyl trisodium diphosphate  
 259793-80-1P, 3-(Chloromethyl)-3-hydroxybutyl trisodium diphosphate  
 259793-81-2P, 3-(Bromomethyl)-3-hydroxybutyl tetrasodium triphosphate  
 259793-82-3P, 3-Hydroxy-3-(iodomethyl)butyl tetrasodium triphosphate  
 259793-83-4P, .alpha.,.gamma.-Bis(3-(bromomethyl)-3-hydroxybutyl) trisodium triphosphate  
 259793-84-5P, .alpha.,.gamma.-Bis(3-hydroxy-3-(iodomethyl)butyl) trisodium triphosphate  
 259793-85-6P, .gamma.-(3-Hydroxy-3-(iodomethyl)butyl) trisodium uridine 5'-triphosphate  
 259793-86-7P, .alpha.,.beta.-Bis(3-(bromomethyl)-3-hydroxybutyl) disodium diphosphate  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(prepn. and activation of T.gamma.9.delta.2 lymphocytes by)

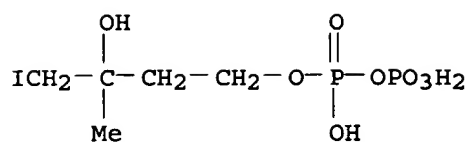
IT 259793-78-7P, 3-(Bromomethyl)-3-hydroxybutyl trisodium diphosphate  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prepn., toxicity and activation of T.gamma.9.delta.2 lymphocytes by)

IT 259793-79-8P, 3-Hydroxy-3-(iodomethyl)butyl trisodium diphosphate  
 259793-80-1P, 3-(Chloromethyl)-3-hydroxybutyl trisodium diphosphate  
 259793-81-2P, 3-(Bromomethyl)-3-hydroxybutyl tetrasodium triphosphate  
 259793-82-3P, 3-Hydroxy-3-(iodomethyl)butyl tetrasodium triphosphate  
 259793-83-4P, .alpha.,.gamma.-Bis(3-(bromomethyl)-3-hydroxybutyl) trisodium triphosphate  
 259793-84-5P, .alpha.,.gamma.-Bis(3-hydroxy-3-(iodomethyl)butyl) trisodium triphosphate  
 259793-85-6P, .gamma.-(3-Hydroxy-3-(iodomethyl)butyl) trisodium uridine 5'-triphosphate  
 259793-86-7P, .alpha.,.beta.-Bis(3-(bromomethyl)-3-hydroxybutyl) disodium diphosphate  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(prepn. and activation of T.gamma.9.delta.2 lymphocytes by)

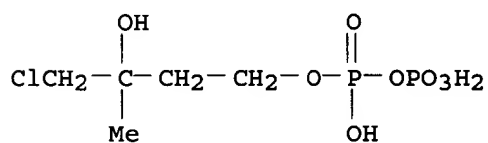
RN 259793-79-8 HCAPLUS

CN Diphosphoric acid, mono(3-hydroxy-4-iodo-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)



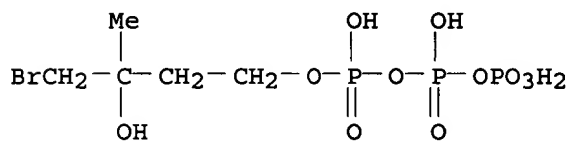
●3 Na

RN 259793-80-1 HCAPLUS  
 CN Diphosphoric acid, mono(4-chloro-3-hydroxy-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)



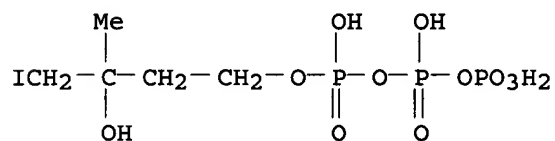
●3 Na

RN 259793-81-2 HCAPLUS  
 CN Triphosphoric acid, P-(4-bromo-3-hydroxy-3-methylbutyl) ester, tetrasodium salt (9CI) (CA INDEX NAME)



●4 Na

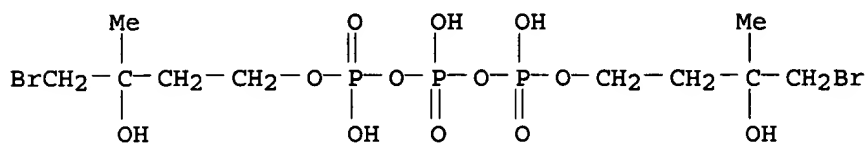
RN 259793-82-3 HCAPLUS  
 CN Triphosphoric acid, P-(3-hydroxy-4-iodo-3-methylbutyl) ester, tetrasodium salt (9CI) (CA INDEX NAME)



●4 Na

RN 259793-83-4 HCAPLUS

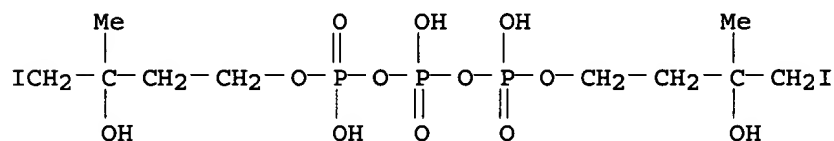
CN Triphosphoric acid, P,P''-bis(4-bromo-3-hydroxy-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)



● 3 Na

RN 259793-84-5 HCAPLUS

CN Triphosphoric acid, P,P''-bis(3-hydroxy-4-iodo-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)

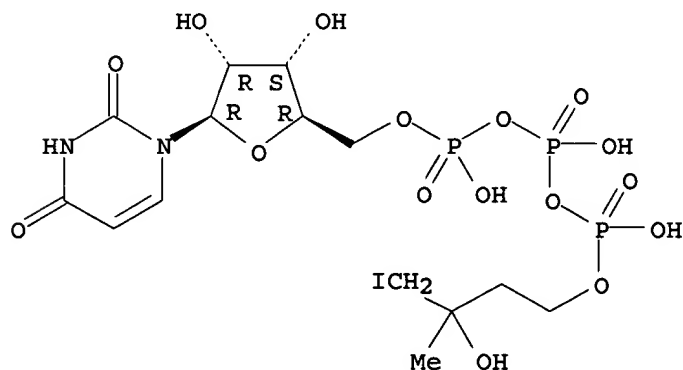


● 3 Na

RN 259793-85-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), P''-(3-hydroxy-4-iodo-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)

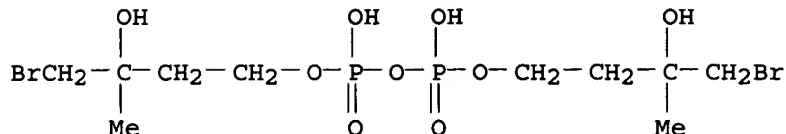
Absolute stereochemistry.



● 3 Na

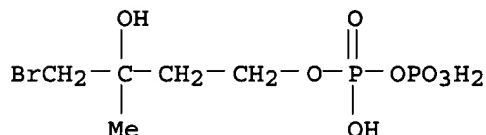
RN 259793-86-7 HCAPLUS

CN Diphosphoric acid, P,P'-bis(4-bromo-3-hydroxy-3-methylbutyl) ester, disodium salt (9CI) (CA INDEX NAME)



●2 Na

IT 259793-78-7P, 3-(Bromomethyl)-3-hydroxybutyl trisodium diphosphate  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prepn., toxicity and activation of T.gamma.9.delta.2 lymphocytes by)  
 RN 259793-78-7 HCAPLUS  
 CN Diphosphoric acid, mono(4-bromo-3-hydroxy-3-methylbutyl) ester, trisodium salt (9CI) (CA INDEX NAME)



●3 Na

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:168920 HCAPLUS

DOCUMENT NUMBER: 122:100378

TITLE: Mechanism of Mevalonate Pyrophosphate Decarboxylase: Evidence for a Carbocationic Transition State

AUTHOR(S): Dhe-Paganon, Sirano; Magrath, Joe; Abeles, Robert H.

CORPORATE SOURCE: Graduate Department of Biochemistry, Brandeis University, Waltham, MA, 02254, USA

SOURCE: Biochemistry (1994), 33(45), 13355-62  
 CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mevalonate pyrophosphate decarboxylase catalyzes the decarboxylation of mevalonate pyrophosphate to isopentyl pyrophosphate. The mechanism of action of this enzyme was investigated to elucidate the mechanism of inhibition by 3-hydroxy-3-(fluoromethyl)-5-pyrophosphopentanoic acid (II). It was previously found that II is a competitive inhibitor ( $K_i = 0.01 \mu\text{M}$ ) of the enzyme reaction [Reardon, J. E., & Abeles, R. H. (1987) Biochem. 26, 4717-4722; Nave, J. F., d'Orchymont, H., Ducep, J. B., Piriou, F., & Jung, M. J. (1985) Biochem. J. 227, 247-254]. We have now obsd. that II is decarboxylated 2500-fold more slowly than mevalonate

pyrophosphate (3-hydroxy-3-methyl-5-pyrophosphopentanoic acid, I). The enzyme was exposed to satg. concns. of II and ATP and then passed through a Penefsky column to remove excess substrate. The enzyme was denatured immediately upon emerging from the Penefsky column. Nearly 1 equiv of both 3-phospho-3-(fluoromethyl)-5-pyrophosphopentanoic acid and ADP was bound to the enzyme. 3-Hydroxy-5-pyrophosphopentanoic acid (III) is phosphorylated at the secondary hydroxyl group and released from the enzyme without decarboxylation. This reaction is 30-fold slower than the rate of decarboxylation of I. The introduction of the 3-fluoromethyl group as well as the removal of the 3-Me group results in low rates of decarboxylation. These substrate analogs have decreased electron d. relative to the tertiary carbon of the substrate. Therefore, the transition state of the decarboxylation step has considerable carbocationic character. Further support for the carbocationic transition state is provided by the finding that N-methyl-N-carboxymethyl-2-pyrophosphoethanolamine (IV) inhibits the enzyme reaction with  $K_i = 0.75$  .mu.M. IV is probably a transition-state analog in which the pos. charged nitrogen atom is analogous to the carbocation.

CC 7-4 (Enzymes)

IT 160556-82-1P 160556-83-2P 160556-86-5P 160556-89-8P

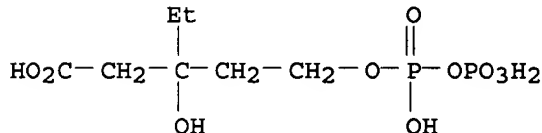
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

IT 160556-89-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 160556-89-8 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanon-9-oic acid, 7-ethyl-1,1,3,7-tetrahydroxy-,  
1,3-dioxide, lithium salt (9CI) (CA INDEX NAME)



●x Li

L9 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:539564 HCAPLUS

DOCUMENT NUMBER: 119:139564

TITLE: Biosynthesis of Archaeobacterial lipids in  
Halobacterium halobium and Methanobacterium  
thermoautotrophicum

AUTHOR(S): Zhang, Donglu; Poulter, C. Dale

CORPORATE SOURCE: Dep. Chem., Univ. Utah, Salt Lake City, UT, 84112, USA

SOURCE: J. Org. Chem. (1993), 58(15), 3919-22

CODEN: JOCEAH; ISSN: 0022-3263

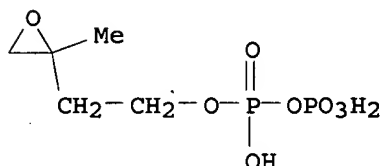
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The core membrane lipids in archaeobacteria are isoprenoid ether derivs., e.g. I, of glycerol instead of fatty acid esters found in other organisms. Activities for three key enzymes in membrane lipid biosynthesis, isopentenyl diphosphate (IPP) isomerase, geranylgeranyl diphosphate (GGPP) synthase, and 3-O-geranylgeranylglyceryl phosphate (GGGP) synthase were found in the cytosolic fractions of cell-free homogenates from the strict

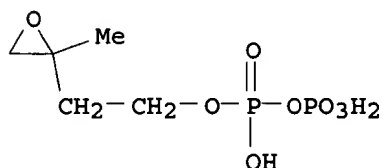
anaerobe Methanobacterium thermoautotrophicum and the extreme halophile Halobacterium halobium. The substrate selectivities of GGGP synthase from both sources were similar and indicate a common pathway for biosynthesis of the isoprenoid compds. in core membrane lipids from methanogenic and halophilic archaebacteria.

CC 30-20 (Terpenes and Terpenoids)  
 Section cross-reference(s): 7  
 IT 19622-70-9P, (R)-[14C]-Glycerol 98755-13-6P 115914-67-5P  
 115914-68-6P 149221-92-1P, [32P]-Dihydroxyacetone phosphate  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. and inhibition by, of isopentenyl diphosphate  
 isomerase)  
 IT 115914-67-5P  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. and inhibition by, of isopentenyl diphosphate  
 isomerase)  
 RN 115914-67-5 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX  
 NAME)

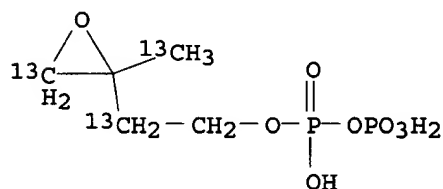


L9 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:587103 HCAPLUS  
 DOCUMENT NUMBER: 117:187103  
 TITLE: Isopentenyl-diphosphate isomerase: irreversible  
 inhibition by 3-methyl-3,4-epoxybutyl diphosphate  
 AUTHOR(S): Lu, Xiang J.; Christensen, Dale J.; Poulter, C. Dale  
 CORPORATE SOURCE: Dep. Chem., Univ. Utah, Salt Lake City, UT, 84112, USA  
 SOURCE: Biochemistry (1992), 31(41), 9955-60  
 CODEN: BICHAW; ISSN: 0006-2960  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Isopentenyl diphosphate isomerase (EC 5.3.3.2) (I) catalyzes the  
 1,3-allylic rearrangement of the homoallylic substrate, isopentenyl  
 diphosphate, to its allylic isomer, dimethylallyl diphosphate. The  
 incubation of yeast I with 3-methyl-3,4-epoxybutyl diphosphate (II)  
 resulted in a time-dependent 1st-order loss of activity characteristics of  
 an active-site-directed irreversible process, where  $k_2 = 0.63 \text{ min}^{-1}$  and  $K_i$   
 $= 0.37 \text{ } \mu\text{M}$ . A 1:1 covalent enzyme-inhibitor (E-I) complex was formed  
 upon incubation with [1-14C]II. Inhibited I was treated with trypsin to  
 give 2 radioactive fragments, which were purified by reversed-phase HPLC  
 on a C18 column. The modified amino acid in each fragment was identified  
 as Cys-139 by sequencing the radiolabeled peptides. The incubation of I  
 with [2,4,5-13C3]II gave a 13C-labeled E-I complex. A 1H-13C  
 heteronuclear multiquantum correlation spectrum had strong cross-peaks at  
 1.2/28 and 2.9/48 ppm, which were assigned to the labeled Me group and C4  
 methylene group, resp., of II. In addn., a weak signal at 2.17/42 ppm may  
 be from the C2 methylene group. A comparison of these chem. shifts with  
 those of a synthetic adduct isolated from treatment of II with cysteine  
 indicated that Cys-139 attacks the C4 atom of II to generate a thioether  
 linkage between the enzyme and the inhibitor.

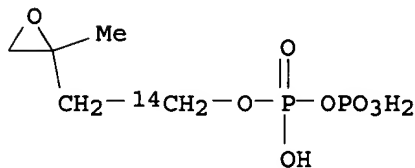
CC 7-3 (Enzymes)  
 IT 115914-67-5  
 RL: BIOL (Biological study)  
 (isopentenyl diphosphate isomerase inhibition by, mechanism of, active site cysteine-139 modification in relation to)  
 IT 143445-82-3P 143445-84-5P  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (**prepn.** and isopentenyl diphosphate isomerase inhibition by)  
 IT 115914-67-5  
 RL: BIOL (Biological study)  
 (isopentenyl diphosphate isomerase inhibition by, mechanism of, active site cysteine-139 modification in relation to)  
 RN 115914-67-5 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX NAME)



IT 143445-82-3P 143445-84-5P  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (**prepn.** and isopentenyl diphosphate isomerase inhibition by)  
 RN 143445-82-3 HCAPLUS  
 CN Diphosphoric acid, mono[2-[2-(methyl-13C)oxiranyl-3-13C]ethyl-2-13C] ester (9CI) (CA INDEX NAME)



RN 143445-84-5 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl-1-14C] ester (9CI) (CA INDEX NAME)



L9 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1988:524850 HCAPLUS  
 DOCUMENT NUMBER: 109:124850  
 TITLE: Isopentenyl-diphosphate isomerase: inactivation of the



enzyme with active-site-directed irreversible inhibitors and transition state analogs  
 AUTHOR(S): Muehlbacher, Manfred; Poulter, C. Dale  
 CORPORATE SOURCE: Dep. Chem., Univ. Utah, Salt Lake City, UT, 84112, USA  
 SOURCE: Biochemistry (1988), 27(19), 7315-28  
 CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Seven analogs of isopentenyl diphosphate and dimethylallyl diphosphate contg. F, epoxy, and ammonium functional groups irreversibly inhibited isopentenyl diphosphate isomerase (EC 5.3.3.2) from *Claviceps purpurea*. Inactivation kinetics, substrate protection studies, and labeling expts. demonstrated that the analogs interacted stoichiometrically with the active site of the enzyme. Radioactive enzyme-inactivator complexes were stable to extended dialysis and treatment with chaotropic reagents. The complexes resulting from inactivation of isomerase by 3-(fluoromethyl)-3-buten-1-yl diphosphate (I) and 3,4-epoxy-3-methyl-1-Bu diphosphate were also stable to ion-exchange chromatog. and gel electrophoresis. Stoichiometric release of F- occurred during inactivation of isomerase with I. This observation was consistent with SN2 or SN2' displacement of F by an active-site nucleophile with concomitant covalent attachment of the inactivator to the enzyme. 2-(Dimethylamino)ethyl diphosphate (II) formed a stable noncovalent complex with isomerase with a dissocn. const. of < 1.2 .times. 10-10M. The enzyme-inhibitor complex was stable in 6M urea, but the inhibitor was partially released upon treatment with SDS and 2-mercaptoethanol at 37.degree. for 1 h. The results indicated that II is a transition-state/reactive intermediate analog where the pos. charged ammonium group mimics a tertiary carbocationic species in the enzyme-catalyzed reaction.

CC 7-3 (Enzymes)

IT 104072-31-3P 115914-80-2P 115914-81-3P 115914-82-4P  
 115914-83-5P 115914-84-6P 115914-85-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and isopentenyl diphosphate isomerase of *Claviceps purpurea* inactivation by)

IT 115914-67-5P 115914-68-6P 115914-69-7P

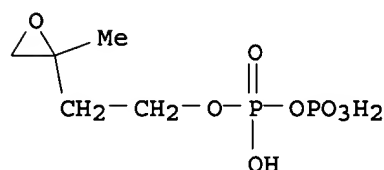
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and kinetics of isopentenyl diphosphate isomerase of *Claviceps purpurea* inactivation by)

IT 115914-82-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and isopentenyl diphosphate isomerase of *Claviceps purpurea* inactivation by)

RN 115914-82-4 HCAPLUS

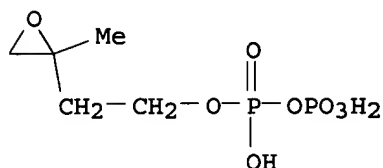
CN Diphosphoric acid, labeled with phosphorus-32, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX NAME)



IT 115914-67-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and kinetics of isopentenyl diphosphate isomerase of *Claviceps purpurea* inactivation by)

RN 115914-67-5 HCAPLUS  
 CN Diphosphoric acid, mono[2-(2-methyloxiranyl)ethyl] ester (9CI) (CA INDEX NAME)



L9 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:108588 HCAPLUS

DOCUMENT NUMBER: 108:108588

TITLE: Studies on pig liver mevalonate-5-diphosphate decarboxylase

AUTHOR(S): Chiew, Yoke Eng; O'Sullivan, William J.; Lee, Choy Soong

CORPORATE SOURCE: Sch. Biochem., Univ. New South Wales, Kensington, 2033, Australia

SOURCE: Biochim. Biophys. Acta (1987), 916(3), 271-8  
 CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A procedure in which 3 sequential enzymes of cholesterol biosynthesis, mevalonate kinase (EC 2.7.1.36), phosphomevalonate kinase (EC 2.7.4.2) and mevalonate-5-diphosphate decarboxylase (EC 4.1.1.33), from pig liver, could be purified in 1 operation is described. Mevalonate kinase and phosphomevalonate kinase were utilized for the enzymic synthesis of mevalonate 5-diphosphate (both 1-<sup>14</sup>C-labeled and unlabeled), the substrate for mevalonate-5-diphosphate decarboxylase, using excess free ATP. A radioactive assay for the enzyme, based on the release of <sup>14</sup>CO<sub>2</sub> from [1-<sup>14</sup>C]mevalonate 5-diphosphate, was developed. The assay allowed reassessment of the metal and nucleotide specificity of the decarboxylase. ATP could be partially replaced by GTP and ITP, but no activity was obsd. with CTP, UTP, or TTP. Apparent activation of the enzyme by ATP was obsd. as found previously for mevalonate kinase and for phosphomevalonate kinase. The presence of 1 mM excess free ATP, above that complexed as the substrate MgATP, decreased the K<sub>m</sub> for MgATP from 0.45 mM to 0.15 mM. MgADP acted as a competitive inhibitor with respect to MgATP.

CC 7-2 (Enzymes)

IT 1492-08-6P 113305-27-4P

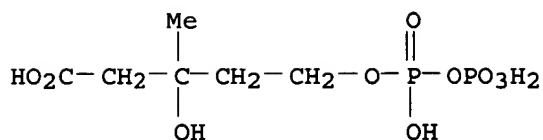
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, enzymic, for mevalonate diphosphate decarboxylase detn.)

IT 1492-08-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, enzymic, for mevalonate diphosphate decarboxylase detn.)

RN 1492-08-6 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide (9CI) (CA INDEX NAME)



L9 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:454274 HCAPLUS

DOCUMENT NUMBER: 107:54274

TITLE: Inhibition of cholesterol biosynthesis by fluorinated mevalonate analogs

AUTHOR(S): Reardon, John E.; Abeles, Robert H.

CORPORATE SOURCE: Grad. Dep. Biochem., Brandeis Univ., Waltham, MA, 02254, USA

SOURCE: Biochemistry (1987), 26(15), 4717-22

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The conversion of mevalonate to cholesterol in rat liver homogenates (50% inhibitory concn. = 0.01-1.0 mM) is inhibited by 6-mono- (I), 6,6-di- (II), and 6,6,6-trifluoromevalonate (III), as well as 4,4-difluoromevalonate (IV). Addn. of compd. I, III, or IV to rat liver homogenates results in the accumulation of 5-phospho- and 5-pyrophosphomevalonate. The conversion of isopentenyl pyrophosphate to cholesterol is not inhibited by the fluorinated analogs. Thus, the decarboxylation of mevalonate 5-pyrophosphate is apparently inhibited. Rat liver homogenates catalyze the phosphorylation of I and III. The inhibition of the decarboxylation of mevalonate 5-pyrophosphate by I and III is demonstrated directly with partially purified decarboxylase. Compd. I is a remarkably effective inhibitor of the decarboxylation ( $K_i = 10 \text{ nM}$ ). It is likely that the phosphorylated or pyrophosphorylated forms of all inhibitors tested are responsible for inhibition. A chem. method for the synthesis of mevalonate 5-pyrophosphate is also described.

CC 6-1 (General Biochemistry)

Section cross-reference(s): 26

IT 1492-08-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and cholesterol formation by liver inhibition by)

IT 108868-99-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation)

(prepn. and demethylation of)

IT 108869-00-7P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and lithium removal from)

IT 108869-01-8P 108869-03-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

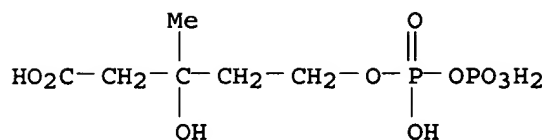
IT 1492-08-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and cholesterol formation by liver inhibition by)

RN 1492-08-6 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide (9CI) (CA INDEX NAME)

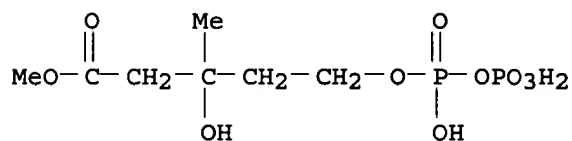


IT 108868-99-1P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation)

(prepn. and demethylation of)

RN 108868-99-1 HCAPLUS

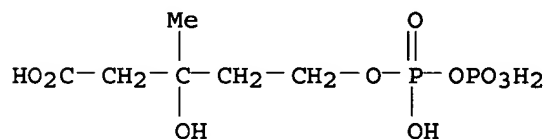
CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
methyl ester, 1,3-dioxide, trilithium salt (9CI) (CA INDEX NAME)

●3 Li

IT 108869-00-7P

RL: SPN (Synthetic preparation); **PREP** (Preparation)  
(prepn. and lithium removal from)

RN 108869-00-7 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
1,3-dioxide, tetralithium salt (9CI) (CA INDEX NAME)

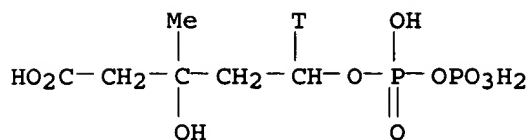
●4 Li

IT 108869-01-8P

RL: SPN (Synthetic preparation); **PREP** (Preparation)  
(prepn. of)

RN 108869-01-8 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic-5-t acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
1,3-dioxide (9CI) (CA INDEX NAME)



L9 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:474858 HCAPLUS

DOCUMENT NUMBER: 105:74858

TITLE: Mevalonate-5-diphosphate decarboxylase:  
stereochemical course of ATP-dependent phosphorylation  
of mevalonate 5-diphosphate

AUTHOR(S): Iyengar, Radha; Cardemil, Emilio; Frey, Perry A.

CORPORATE SOURCE: Dep. Quim., Univ. Santiago, Santiago, Chile

SOURCE: Biochemistry (1986), 25(16), 4693-8

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chicken liver mevalonate 5-diphosphate carboxylase catalyzes the reaction of mevalonate 5-diphosphate (MVADP) with ATP to produce isopentenyl diphosphate, ADP, CO<sub>2</sub>, and inorg. phosphate. The overall reaction involves an anti elimination of the tertiary hydroxyl and carboxyl groups. To investigate the mechanism for transfer of the terminal phosphoryl group of ATP to the C-3 O atom of MVADP, the reaction was carried out using stereospecifically labeled (SP)-adenosine 5'-O-(3-thio[3-1702,180]triphosphate) ([.gamma.-1702,180]ATP.gamma.S) in place of ATP. The configuration of the [170,180]thiophosphate produced was found to be RP, corresponding to overall inversion of configuration at the P atom in the thiophosphoryl group transfer step. This result was consistent with the direct transfer of the thiophosphoryl group from (SP)-[.gamma.-1702,180]ATP.gamma.S to MVADP at the active site. The result did not indicate the involvement of a covalent thiophosphoryl-enzyme on the reaction pathway.

CC 7-4 (Enzymes)

IT 56-65-5, reactions 103025-21-4

RL: RCT (Reactant)

(reaction of, with mevalonate diphosphate decarboxylase, stereochem. of)

IT 103025-21-4

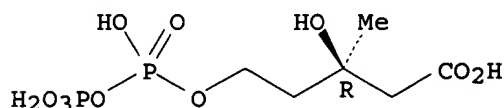
RL: RCT (Reactant)

(reaction of, with mevalonate diphosphate decarboxylase, stereochem. of)

RN 103025-21-4 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide, (R)- (9CI) (CA INDEX NAME)

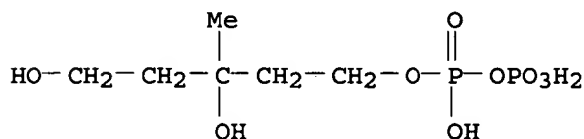
Absolute stereochemistry.



L9 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:574788 HCAPLUS

DOCUMENT NUMBER: 103:174788  
 TITLE: Separation of mevalonate phosphates and isopentenyl pyrophosphate by thin-layer chromatography and of short-chain prenyl phosphates by ion-pair chromatography on a high-performance liquid chromatography column  
 AUTHOR(S): Beyer, Peter; Kreuz, Klaus; Kleinig, H.  
 CORPORATE SOURCE: Inst. Biol., Univ. Freiburg, Freiburg, D-7800, Fed. Rep. Ger.  
 SOURCE: Methods Enzymol. (1985), 111 (Steroids Isoprenoids, Part B), 248-52  
 CODEN: MENZAU; ISSN: 0076-6879  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A 2-dimensional TLC system is described that can sep. clearly mevalonate, mevalonate phosphate, mevalonate pyrophosphate, and isopentenyl pyrophosphate. The 1st dimension developer is  $\text{PrOH:NH}_3$  (25% aq. soln.): $\text{H}_2\text{O}$  (6:3:1), and the 2nd dimension developer is  $\text{iso-BuOH:AcOH:H}_2\text{O}$  (40:10:13). The compds. can be detected with a radioscaner or by autoradiog. and quantified by scintillation counting. A method is also presented which allows the sepn. of geranyl, farnesyl, and geranylgeranyl mono- and pyrophosphates very rapidly by ion-pair reversed-phase HPLC. The ion-pair reagent contains tetrabutylammonium sulfate 6.8 g and  $\text{K}_2\text{HPO}_4$  5.5 g, adjusted to pH 8.0 with KOH in a total vol. of 100 mL  $\text{H}_2\text{O}$ . The reagent is filtered through Millipore HA filters (0.45  $\mu\text{m}$ ). For sepn., a HPLC system equipped with a C18 reversed-phase column ( $\mu\text{Bondapak C18}$ ) and a radio column chromatog. monitor with a glass scintillator is used. The column is developed with a 15-min linear gradient ranging from 15% nonpolar solvent/85% polar solvent to 70% nonpolar solvent/30% polar solvent at a flow rate of 1.3 mL/min. Under these conditions, the decrease in polarity of the eluent is paralleled by a decrease in the concn. of ion-pair reagent which allows the resoln. of mono- and pyrophosphates of the higher homologs.  
 CC 9-3 (Biochemical Methods)  
 IT 150-97-0 358-71-4 89600-14-6 98775-29-2  
 RL: PROC (Process)  
 (sepn. of, by TLC)  
 IT 98775-29-2  
 RL: PROC (Process)  
 (sepn. of, by TLC)  
 RN 98775-29-2 HCAPLUS  
 CN Diphosphoric acid, mono(3,5-dihydroxy-3-methylpentyl) ester (9CI) (CA INDEX NAME)



L9 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1979:570587 HCAPLUS  
 DOCUMENT NUMBER: 91:170587  
 TITLE: Effect of phenyl and phenolic acids on mevalonate-5-phosphate kinase and mevalonate-5-pyrophosphate decarboxylase of the rat brain  
 AUTHOR(S): Bhat, Charavu Shama; Ramasarma, T.

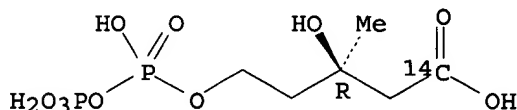
CORPORATE SOURCE: Dep. Biochem., Indian Inst. Sci., Bangalore, India  
 SOURCE: J. Neurochem. (1979), 32(5), 1531-7  
 CODEN: JONRA9; ISSN: 0022-3042

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Ph and phenolic acids inhibited metab. of mevalonate in rat brain by inhibition of mevalonate 5-pyrophosphate decarboxylase (EC 4.1.1.33) (I); phenolic acids also inhibited mevalonate 5-phosphate kinase (EC 2.7.4.2) (II) on preincubation. Inhibition kinetics showed that p-coumaric and isoferulic acids competed with the substrates, mevalonate 5-phosphate or mevalonate 5-pyrophosphate, whereas other acids showed a noncompetitive type of inhibition. Chlorophenoxyisobutyrate did not affect I or II.

CC 7-3 (Enzymes)  
 IT 71816-03-0P 71816-04-1P  
 RL: SPN (Synthetic preparation); **PREP** (Preparation)  
 (prepn. of)  
 IT 71816-04-1P  
 RL: SPN (Synthetic preparation); **PREP** (Preparation)  
 (prepn. of)  
 RN 71816-04-1 HCAPLUS  
 CN 2,4-Dioxa-1,3-diphosphanonan-9-oic-9-14C acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1976:1328 HCAPLUS  
 DOCUMENT NUMBER: 84:1328  
 TITLE: Phosphorylation of homomevalonic acid by an enzyme system from rat liver

AUTHOR(S): Beedle, Alan S.; Rees, Huw H.; Goodwin, Trevor W.  
 CORPORATE SOURCE: Dep. Biochem., Univ. Liverpool, Liverpool, Engl.  
 SOURCE: Biochem. Soc. Trans. (1975), 3(5), 738-9  
 CODEN: BCSTB5

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Incubation of mevalonic acid with rat liver postmicrosomal supernatant yielded mainly farnesyl pyrophosphate, and also mevalonate 5-phosphate, mevalonate 5-pyrophosphate, and isopentenyl pyrophosphate. Homomevalonic acid incubated under the same conditions gave homomevalonate 5-pyrophosphate, and some homomevalonate 5-phosphate. Homoisoprenoid pyrophosphates were not detected possibly because of the presence of an extra Me group at the C-3 creating steric hindrance around the C-3 OH group and preventing recognition by mevalonate 5-pyrophosphate anhydrodecarboxylase.

CC 6-1 (General Biochemistry)  
 Section cross-reference(s): 7

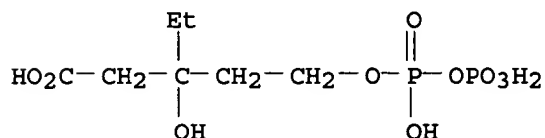
IT 58084-40-5P  
 RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP** (Preparation)  
 (formation of, by liver enzyme system)

IT 58084-40-5P  
 RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); **PREP (Preparation)**  
(formation of, by liver enzyme system)

RN 58084-40-5 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 7-ethyl-1,1,3,7-tetrahydroxy-,  
1,3-dioxide (9CI) (CA INDEX NAME)



L9 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1974:564916 HCAPLUS

DOCUMENT NUMBER: 81:164916

TITLE: Metabolism of mevalonic acid to phosphorylated  
intermediates in a cell-free extract from Nepeta  
cataria leaves

AUTHOR(S): Downing, Michael R.; Mitchell, Earl D.

CORPORATE SOURCE: Agric. Exp. Stn., Oklahoma State Univ., Stillwater,  
Okla., USA

SOURCE: Phytochemistry (1974), 13(8), 1419-21  
CODEN: PYTCAS

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A cell-free ext. was prepd. from leaves of N. cataria plants which  
converted mevalonic acid to mevalonic acid phosphate, mevalonic acid  
pyrophosphate, and isopentenyl pyrophosphate. These enzymes were in the  
30,000 g supernatant. The activities were maximal at pH 7 and the  
formation of mevalonic acid pyrophosphate and isopentenyl pyrophosphate  
reached a max. after an incubation time of 180 min, whereas the level of  
mevalonic acid phosphate began to decrease after 90 min.

CC 6-1 (General Biochemistry)  
Section cross-reference(s): 11

IT 358-71-4P 1189-94-2P 1492-08-6P

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,  
nonpreparative); **PREP (Preparation)**

(formation of, by Nepeta cataria leaves, mevalonic acid in relation to)

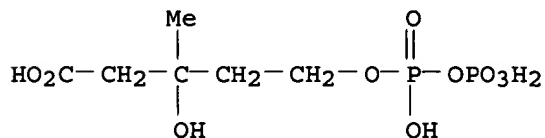
IT 1492-08-6P

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,  
nonpreparative); **PREP (Preparation)**

(formation of, by Nepeta cataria leaves, mevalonic acid in relation to)

RN 1492-08-6 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
1,3-dioxide (9CI) (CA INDEX NAME)

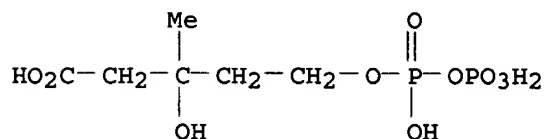


L9 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1971:400161 HCAPLUS



DOCUMENT NUMBER: 75:161  
 TITLE: Rate of acetate and mevalonate incorporation by extracts of Pinus pinaster seedlings  
 AUTHOR(S): Garcia-Peregrin, E.; Mayor, F.  
 CORPORATE SOURCE: Dep. Biochem., Univ. Granada, Granada, Spain  
 SOURCE: Rev. Espan. Fisiol. (1971), 27(1), 15-22  
 CODEN: REFIAS  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The conditions were studied for obtaining cell-free exts. of pine seedlings incorporating acetate and mevalonate. The whole sequence of reactions which relate acetate to active isoprene in pine seems to be identical to the pathway in animal cells and microorganisms. Acetate is incorporated by enzymes in the ext. and is transformed into mevalonic acid derivs. Incorporation occurs only when CoA-SH and glutathion are added. In the absence of CoA-SH, the reaction rate is very slow and its intensity is greatly reduced when NADPH is not supplied. Addn. of malonate has no effect on the reaction. Incorporation was demonstrated of mevalonate by cell-free exts. of P. pinaster seedlings. The addn. of F to the reaction mixt. to inhibit phosphates prevents its action on phospho- and pyrophosphomevalonic acid and allows a greater accumulation of intermediates and a better visualization of the reactions of the metabolic system. The rate of incorporation of mevalonate-1-14C and mevalonate-2-14C is extremely rapid. Highest levels of phospho- and pyrophosphomevalonate are found after 15-30 min. As incubation time increases (0-10 hr) the production of further metabolites (possibly geranyl or neryl pyrophosphate) also increases.  
 CC 2 (General Biochemistry)  
 IT 358-71-4P 1189-94-2P 1492-08-6P  
 RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)  
 (formation of, in acetic acid metabolism by pine)  
 IT 1492-08-6P  
 RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)  
 (formation of, in acetic acid metabolism by pine)  
 RN 1492-08-6 HCAPLUS  
 CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide (9CI) (CA INDEX NAME)



L9 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1969:84400 HCAPLUS  
 DOCUMENT NUMBER: 70:84400  
 TITLE: Biosynthesis of cholesterol by the bovine aorta and the mechanism of action of .alpha.-(p-chlorophenoxy)isobutyric acid  
 AUTHOR(S): Walsh, Maria R.; Teal, Stephen W.; Gamble, Wilbert  
 CORPORATE SOURCE: Oregon State Univ., Corvallis, Oreg., USA  
 SOURCE: Arch. Biochem. Biophys. (1969), 130(1), 7-18  
 CODEN: ABBIA4  
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB The nature and requirements for the biosynthesis of nonsaponifiable material (NSF) and cholesterol from acetate-2-14C, acetyl-1-14C CoA and mevalonate-2-14C by cell-free systems from bovine aorta were detd. Low radioactivity was incorporated into cholesterol with mevalonate as substrate. No conversion of acetate to NSF and cholesterol was observed; however, acetyl-CoA was converted to NSF. Bovine aorta cellfree systems were shown to convert mevalonate to mevalonic acid-5-phosphate and mevalonic acid-5-pyrophosphate. The majority of the radioactivity was incorporated into a compd. tentatively identified as a polar isoprenoid. Mevalonate conversion to NSF and cholesterol was inhibited by .alpha.-p-chlorophenoxyisobutyrate (CPIB) and related compds. Mevalonate kinase was inhibited by CPIB. The inhibition of mevalonate incorporation was prevented by increasing the ATP concn. CPIB inhibited the biosynthesis of fatty acids by homogenates of bovine aorta and the conversion of acetate to CO2.

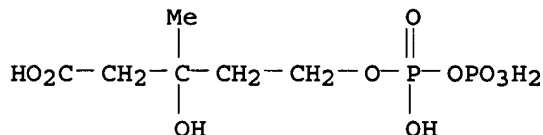
CC 2 (General Biochemistry)

IT 1189-94-2P 1492-08-6P  
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**  
(formation of, from mevalonic acid by arteries)

IT 1492-08-6P  
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**  
(formation of, from mevalonic acid by arteries)

RN 1492-08-6 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanon-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-, 1,3-dioxide (9CI) (CA INDEX NAME)



L9 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1967:72582 HCAPLUS

DOCUMENT NUMBER: 66:72582

TITLE: Phosphorylated intermediates in the biosynthesis of terpenes in a soluble system (homogenate) of Pinus radiata seedlings

AUTHOR(S): Beytia Simpson, Enrique

SOURCE: An. Fac. Quim. Farm., Univ. Chile (1966), Volume Date 1965, 17, 119-23

CODEN: AFQFAU

DOCUMENT TYPE: Journal

LANGUAGE: Spanish

AB Cell-free exts. obtained by centrifugation of a homogenate prepd. from P. radiata seedlings incorporate labeled mevalonic acid into 5-phosphomevalonic acid, 5-pyrophosphomevalonic acid, and isopentenyl 1-pyrophosphate. Part of the radioactivity in the petroleum ether-sol. fraction was found after hydrolysis with N HCl, suggesting the formation of allyl pyrophosphates. Mevalonic acid kinase of these exts. is stereospecific with one of the enantiomorphous forms of mevalonic acid, is activated by Mn2+, and is inhibited by EDTA. 21 references.

CC 2 (General Biochemistry)

IT 358-72-5P 1492-08-6P

RL: PREP (Preparation)

(formation by Pinus radiata, in terpene formation)

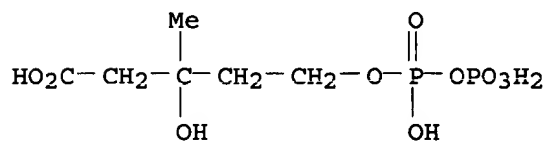
IT 1492-08-6P

RL: PREP (Preparation)

(formation by Pinus radiata, in terpene formation)

RN 1492-08-6 HCAPLUS

CN 2,4-Dioxa-1,3-diphosphanonan-9-oic acid, 1,1,3,7-tetrahydroxy-7-methyl-,  
1,3-dioxide (9CI) (CA INDEX NAME)



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L10 ANSWER 1 OF 3 HCAOLD COPYRIGHT 2002 ACS  
 AN CA65:9204f CAOLD  
 TI biosynthesis of cholesterol - (XX) steric course of decarboxylation of 5-pyrophosphomevalonate and of the C to C bond formation in the biosynthesis of farnesyl pyrophosphate  
 AU Cornforth, John W.; Cornforth, R. H.; Popjak, G. J.; Yengoyan, L. S.  
 IT 358-71-4 358-72-5 372-97-4 763-10-0 10371-61-6 10371-62-7  
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 13002-30-7 13048-01-6 13100-81-7 89798-87-8 92876-32-9  
 94115-33-0

L10 ANSWER 2 OF 3 HCAOLD COPYRIGHT 2002 ACS  
 AN CA64:5460h CAOLD  
 TI stereochemistry of rubber biosynthesis  
 AU Archer, Bernard L.; Barnard, D.; Cockbain, E. G.; Cornforth, J. W.; Cornforth, R. H.; Popjak, G. J.  
 IT 358-71-4 372-97-4 1492-08-6 5826-34-6  
 5948-92-5

L10 ANSWER 3 OF 3 HCAOLD COPYRIGHT 2002 ACS  
 AN CA61:2959d CAOLD  
 TI synthesis of DL-mevalonic acid pyrophosphate  
 AU Machleidt, Hans; Cohnen, E.; Tschesche, R.  
 IT 1492-08-6 33598-51-5 91675-20-6 91823-84-6 92062-91-4 92274-32-3  
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